Am J Physiol Heart Circ Physiol 301: H1389–H1395, 2011.
First published July 29, 2011; doi:10.1152/ajpheart.00443.2011.

Improved pulse transit time estimation by system identification analysis of proximal and distal arterial waveforms

Da Xu,[1] Kathy L. Ryan,[2] Caroline A. Rickards,[3] Guanqun Zhang,[1] Victor A. Convertino,[2] and Ramakrishna Mukkamala[1]

[1]*Michigan State University, East Lansing, Michigan;* [2]*United States Army Institute of Surgical Research, Fort Sam Houston; and* [3]*University of Texas at San Antonio, San Antonio, Texas*

Submitted 3 May 2011; accepted in final form 25 July 2011

Xu D, Ryan KL, Rickards CA, Zhang G, Convertino VA, Mukkamala R. Improved pulse transit time estimation by system identification analysis of proximal and distal arterial waveforms. *Am J Physiol Heart Circ Physiol* 301: H1389–H1395, 2011. First published July 29, 2011; doi:10.1152/ajpheart.00443.2011.—We investigated the system identification approach for potentially improved estimation of pulse transit time (PTT), a popular arterial stiffness marker. In this approach, proximal and distal arterial waveforms are measured and respectively regarded as the input and output of a system. Next, the system impulse response is identified from all samples of the measured input and output. Finally, the time delay of the impulse response is detected as the PTT estimate. Unlike conventional foot-to-foot detection techniques, this approach is designed to provide an artifact robust estimate of the true PTT in the absence of wave reflection. The approach is also applicable to arbitrary types of arterial waveforms. We specifically applied a parametric system identification technique to noninvasive impedance cardiography (ICG) and peripheral arterial blood pressure waveforms from 15 humans subjected to lower-body negative pressure. We assessed the technique through the correlation coefficient (r) between its 1/PTT estimates and measured diastolic pressure (DP) per subject and the root mean squared error (RMSE) of the DP predicted from these estimates and measured DP. The technique achieved average r and RMSE values of 0.81 ± 0.16 and 4.3 ± 1.3 mmHg. For comparison, the corresponding values were 0.59 ± 0.37 ($P < 0.05$) and 5.9 ± 2.5 ($P < 0.01$) mmHg for the conventional technique applied to the same waveforms and 0.28 ± 0.40 ($P < 0.001$) and 7.2 ± 1.8 ($P < 0.001$) mmHg for the conventional technique with the ECG waveform substituted for the ICG waveform. These results demonstrate, perhaps for the first time, that the system identification approach can indeed improve PTT estimation.

arterial blood pressure; arterial stiffness; foot-to-foot detection; impulse response; pulse wave velocity

ACCORDING TO THE MOENS-KORTEWEG equation, pulse wave velocity (PWV) increases as the arteries stiffen. Indeed, PWV is the most popular index of arterial stiffness because of the ease of its measurement and its proven independent value in predicting cardiovascular events and mortality in hypertensive patients (2, 4, 12, 14). In addition, because arterial stiffness increases with arterial blood pressure (ABP), PWV and ABP often show positive correlation, suggesting that PWV could provide a means to achieve continuous, noninvasive, and cuffless ABP monitoring (18).

Conventionally, PWV is determined from the distance and pulse transit time (PTT) between proximal and distal arterial sites (5). PTT is, in turn, estimated by acquiring arterial waveforms from the two sites and then detecting the foot-to-foot time delay between the waveforms. The premise is that the foot of the proximal waveform represents a time before the return of the reflected wave to its measurement site. However, wave reflection may not always be negligible at the proximal waveform foot. Just as important, it is often difficult to detect the waveform feet reliably because of motion and other artifact (16). Thus, the foot-to-foot detection technique can yield inaccurate PTT estimates. Compounding matters, ABP changes perturb PWV relatively little (18). Thus, typical plots of ABP vs. PWV show significant vertical scatter about the line of best fit (18). This scatter limits the ability of PWV to track ABP.

Several investigators have aimed to improve PTT estimation by more sophisticated analysis of proximal and distal arterial waveforms. Sola et al. (21) applied parametric modeling to the systolic upstrokes of the waveforms to identify their feet more reliably. Pruett et al. (18) computed an average of multiple time delays taken from the early systolic samples of two ABP waveforms to establish PTT estimates that were able to reduce the scatter in ABP vs. PWV plots. While their idea of mitigating PTT error by using more than one pair of samples of the waveforms is interesting, wave reflection becomes a greater factor as the cardiac cycle progresses. This technique is also restricted to ABP and flow waveforms. Latson et al. applied nonparametric system identification to estimate the impulse response (time domain version of the transfer function) relating a proximal ABP waveform (input) to a distal ABP waveform (output) and then estimated PTT as its time delay (11). Their intriguing idea was that, since the impulse response represents the distal ABP response to a very narrow pulse applied to proximal ABP at *time 0*, this PTT estimate should not be corrupted by wave reflection. However, neither Latson et al. nor an ensuing group who reproduced their technique (17) showed that it actually improved PTT estimation. Furthermore, this approach is applicable to arbitrary arterial waveforms (rather than being limited to ABP waveforms) and should afford great robustness to artifact, since PTT is determined from all pairs of waveform samples. However, these latter ideas may have not been noted until now.

We investigated the system identification approach for PTT estimation. We specifically applied a robust parametric system identification technique to an impedance cardiography (ICG) waveform (the proximal input) and a noninvasive peripheral ABP waveform (the distal output) recorded from humans subjected to progressive reductions in central blood volume using a lower-body negative pressure (LBNP) protocol. Because it is difficult to independently measure the true PTT in the absence of wave reflection, we assessed the technique

Address for reprint requests and other correspondence: R. Mukkamala, Dept. of Electrical and Computer Engineering, Michigan State Univ., 2120 Engineering Bldg., East Lansing, MI 48824-1226 (e-mail: rama@egr.msu.edu).

Report Documentation Page

Form Approved
OMB No. 0704-0188

1. REPORT DATE	2. REPORT TYPE	3. DATES COVERED
01 OCT 2011	**N/A**	**-**

4. TITLE AND SUBTITLE	5a. CONTRACT NUMBER
Improved pulse transit time estimation by system identification analysis of proximal and distal arterial waveforms	5b. GRANT NUMBER
	5c. PROGRAM ELEMENT NUMBER
6. AUTHOR(S)	5d. PROJECT NUMBER
Xu D., Ryan K. L., Rickards C. A., Zhang G., Convertino V. A., Mukkamala R.,	5e. TASK NUMBER
	5f. WORK UNIT NUMBER
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)	8. PERFORMING ORGANIZATION REPORT NUMBER
United States Army Institute of Surgical Research, JBSA Fort Sam Houston, TX	
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)	10. SPONSOR/MONITOR'S ACRONYM(S)
	11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION/AVAILABILITY STATEMENT
Approved for public release, distribution unlimited

13. SUPPLEMENTARY NOTES

14. ABSTRACT

15. SUBJECT TERMS

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			
unclassified	**unclassified**	**unclassified**	**UU**	**7**	

in terms of the ability of its (proportional) PWV estimates to track ABP changes. Our results show that the technique greatly reduced the scatter in ABP vs. PWV plots compared with conventional foot-to-foot detection techniques. A preliminary version of this study has been reported in abbreviated form (23).

MATERIALS AND METHODS

Physiological data. Existing, deidentified physiological data from humans subjected to a LBNP protocol were analyzed. The data collection procedures were approved by the Institutional Review Board of the Brooke Army Medical Center (Fort Sam Houston, TX) and are described in detail in several recent publications (7, 20).

Briefly, fit and typically young subjects that showed no signs of cardiovascular abnormalities (e.g., hypertension, hypotension, autonomic nervous dysfunction) and were not pregnant or taking any medications known to alter autonomic nervous function were studied. The subjects were instrumented for measurement of various physiological data, including noninvasive stroke volume estimates via ICG, a noninvasive peripheral ABP waveform via finger-cuff photoplethysmography, and an ECG waveform. Subjects were positioned supine in a LBNP chamber. The data were then recorded at a sampling rate of 500 Hz during *1*) a 5-min baseline period; *2*) 5-min chamber decompression at −15, −30, −45, and −60 mmHg each; *3*) additional increments of −10 mmHg for 5 min until the onset of hemodynamic decompensation [as indicated by presyncopal symptoms, sudden fall in ABP or heart rate (HR), systolic pressure (SP) <80 mmHg, or at the subject's request]; and *4*) a 10-min recovery period.

For this study, 15-s steady segments of data during the baseline period, each distinct LBNP period, and the recovery period were extracted. Because PWV estimates would be assessed in terms of their ability to track ABP changes, appreciable changes in ABP within a subject were needed for the assessment to be challenging and useful. Thus, data from subjects with more modest diastolic pressure (DP) changes (maximum average DP over the periods minus the minimum average DP over the periods <20 mmHg) were excluded. Data from 15 of 66 available subjects (nine males and six females; age 31 ± 8 yr; height 173 ± 12 cm; weight 76 ± 15 kg) remained for analysis.

PTT estimation. PTT was estimated by applying conventional foot-to-foot detection techniques to the simultaneous pairs of the 15-s segments of the differentiated ICG waveform (a proximal arterial waveform that is specifically related to thoracic flow) or the ECG waveform (a commonly proposed surrogate for the proximal arterial waveform) and the peripheral ABP waveform (a distal arterial waveform). PTT was then estimated by applying a parametric system identification technique to the same pairs of ICG and peripheral ABP waveform segments.

Conventional foot-to-foot detection techniques. Figure 1 shows the conventional foot-to-foot detection techniques. First, the waveform feet were detected as the R waves for the ECG waveform, the standard B points for the ICG waveform (i.e., the time of zero derivative before the peak) (22), and the minima for the peripheral ABP waveform (i.e., DP). These foot detection techniques yielded the best results among a set of conventional techniques (6) and are thus referred to as optimized henceforth. Next, the time delays between each R wave and subsequent DP (T_{d1}) and between each B point and ensuing DP (T_{d2}) were determined. Finally, the time delays were averaged over the 15-s waveform segments to reduce noise in the PTT estimates.

Parametric system identification technique. Figure 2 shows the parametric system identification technique. The differentiated ICG waveform was considered to be the input [$x(t)$] to a system while the peripheral ABP waveform [$y(t)$] was regarded as the resulting output. The system was identified by finding its impulse response [$h(t)$], which when convolved with $x(t)$, optimally fitted $y(t)$. The time delay of h(t) (T_{d3}) was then detected as the estimate of PTT. This estimate may be viewed as the time delay for a very narrow pulse of thoracic flow to reach the peripheral ABP measurement site or the time delay between the entire ICG and peripheral ABP waveforms after equalizing their shapes. Mathematical details are provided immediately below.

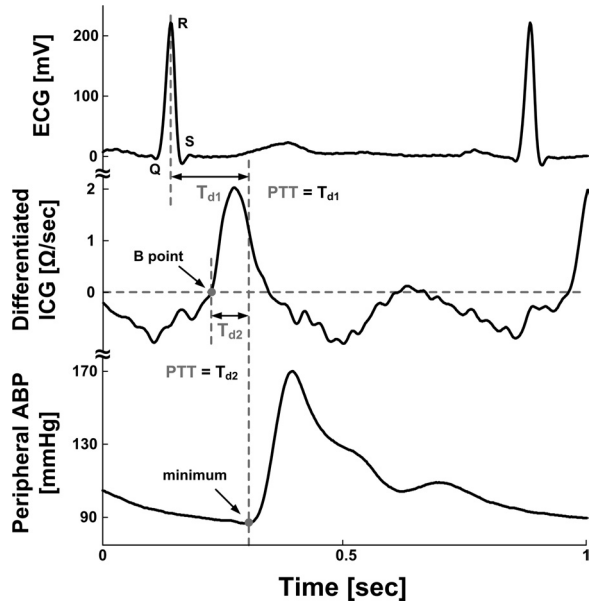

Fig. 1. Optimized conventional foot-to-foot detection techniques for estimating pulse transit time (PTT) from either an ECG or impedance cardiography (ICG) waveform (a proximal waveform) and a simultaneous noninvasive peripheral arterial blood pressure (ABP) waveform (a distal waveform) [the time delays between each R wave and subsequent DP (T_{d1}) and between each B point and ensuing DP (T_{d2})].

The impulse response $h(t)$ was estimated as per the following autoregressive exogenous input structure:

$$y(t) = \sum_{k=1}^{n} a_k y(t-k) + \sum_{k=0}^{m} b_k x(t-k) + e(t),$$

where a_k and b_k are sets of unknown parameters that define $h(t)$, n and m denote the number of parameters in the sets, and $e(t)$ is the unmeasured residual error (13). The term n had little effect on the results and was arbitrarily fixed to five, whereas the term m should scale with PTT and was simply set to T_{d2} times the sampling rate. The parameters were then estimated from the 15-s segments of $x(t)$ and zero-mean $y(t)$ by linear least-squares minimization of $e(t)$ (13). The time delay T_{d3} was thereafter determined as the time of the maximal second derivative of $h(t)$ between its first zero-crossover with positive derivative and its peak. This time, which denotes when the slope of $h(t)$ is changing most during its rise to the peak, provided a good marker of the foot location of $h(t)$ (6). [Determining T_{d3} as the first zero-crossover with positive derivative, which indicates when $h(t)$ first becomes positive as it rises to the peak, yielded similar results.]

PTT assessment and comparison. The PTT estimates of each technique were assessed based on their ability to track the average DP of the analyzed peripheral ABP waveform segments in each subject. Figure 3 shows the PTT assessment procedure. First, since PWV generally shows better linear correlation to DP than PTT, the reciprocals of the PTT estimates were first taken to arrive at proportional PWV estimates per subject. (Note that the proportionality constant, which represents the distance between the proximal and distal arterial sites, was not needed here.) Next, two quantitative metrics were computed. One metric was the standard correlation coefficient (r) between the proportional PWV estimates and measured DP. The other metric was the root mean squared error (RMSE) between the DP predicted by mapping the proportional PWV estimates through the

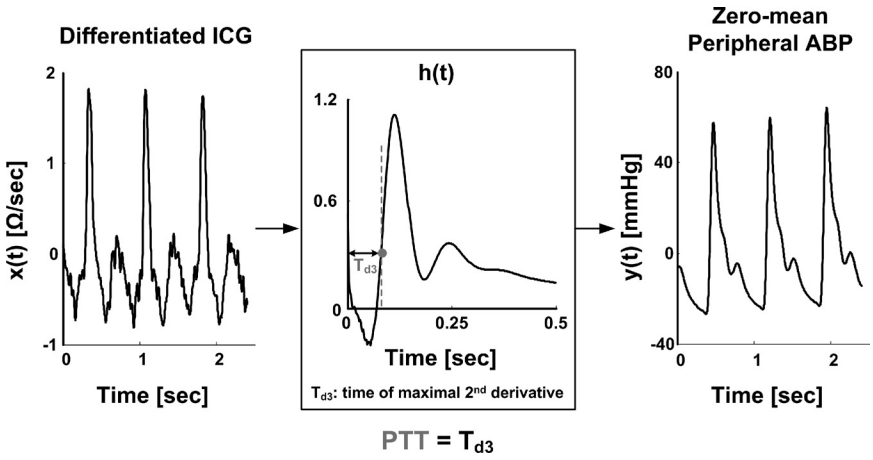

Fig. 2. Parametric system identification technique for estimating PTT from simultaneous ICG and noninvasive peripheral ABP waveforms. First, the former waveform is regarded as an input [$x(t)$] to a system while the latter waveform is considered to be the resulting output [$y(t)$]. Next, the system is identified by finding a parametric impulse response [$h(t)$] (see equation in MATERIALS AND METHODS) that, when convolved with $x(t)$, optimally fits $y(t)$. Finally, the time delay (T_{d3}) of $h(t)$ is detected as the time of its maximal second derivative so as to yield as an estimate of PTT.

line of best fit established from the correlation analysis and the measured DP.

The PTT estimates of the techniques were then statistically compared. Straightforward one-way repeated-measures ANOVA was specifically employed to compare the subject average r values and log-transformed RMSE values of the three techniques. Because both of these tests revealed $P < 0.05$, multiple pairwise comparisons between all techniques were then performed using the Student-Newman-Keuls post hoc test.

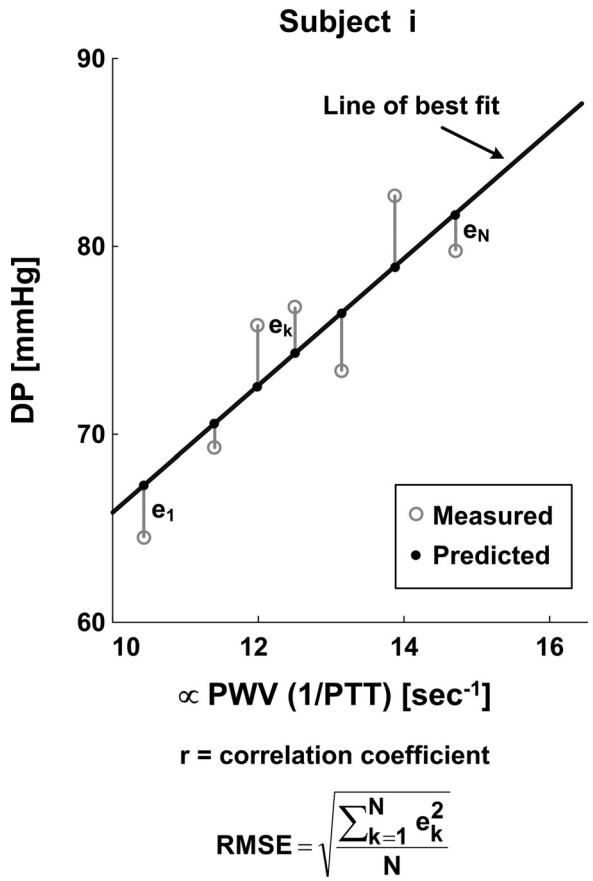

Fig. 3. Procedure for evaluating the PTT estimates of the techniques in terms of their ability to track diastolic pressure (DP) within a subject. Note that 1/PTT here is simply proportional to pulse wave velocity (PWV). RMSE is the root mean squared error.

RESULTS

Figure 4 shows sample plots of measured DP vs. the proportional PWV estimated by each technique from *subjects 15* and *12*. In *subject 15*, the parametric system identification technique noticeably reduced the scatter about the line of best fit compared with the conventional foot-to-foot detection techniques, especially with the ECG waveform substituted for the ICG waveform. In *subject 12*, the conventional techniques produced proportional PWV estimates that showed nonphysiological, negative correlation with DP, whereas the system identification technique yielded estimates that revealed the expected positive correlation.

Figure 5 shows plots of the DP predicted by each technique vs. measured DP from all 15 subjects and the corresponding overall RMSE values (i.e., the root mean square of the errors pooled together from all of the subjects). The system identification technique showed better predictions than both of the conventional techniques.

Table 1 shows the DP range and r and RMSE values of each technique per subject. The average r and RMSE values of the system identification technique were 0.81 ± 0.16 and 4.3 ± 1.3 mmHg. For comparison, the corresponding values were 0.59 ± 0.37 ($P < 0.05$) and 5.9 ± 2.5 ($P < 0.01$) mmHg for the conventional technique applied to the same waveforms and 0.28 ± 0.40 ($P < 0.001$) and 7.2 ± 1.8 ($P < 0.001$) mmHg for the conventional technique with the ECG waveform substituted for the ICG waveform. [Although not indicated in Table 1, the r and RMSE values of the two conventional techniques were also statistically different ($P < 0.05$).] Furthermore, of the 15 r values corresponding to each subject, only 3 were <0.80 for the system identification technique compared with 8 and 15 for the conventional techniques.

DISCUSSION

In summary, PWV is a useful marker of arterial stiffness and may permit continuous, noninvasive, and cuffless ABP monitoring. Conventionally, PWV is determined as the ratio of the distance and PTT between proximal and distal arterial sites. PTT is, in turn, estimated by detecting the foot-to-foot time delay between waveforms measured at the two arterial sites of interest. However, this technique can provide inaccurate PTT estimates because of wave reflection interference and wave-

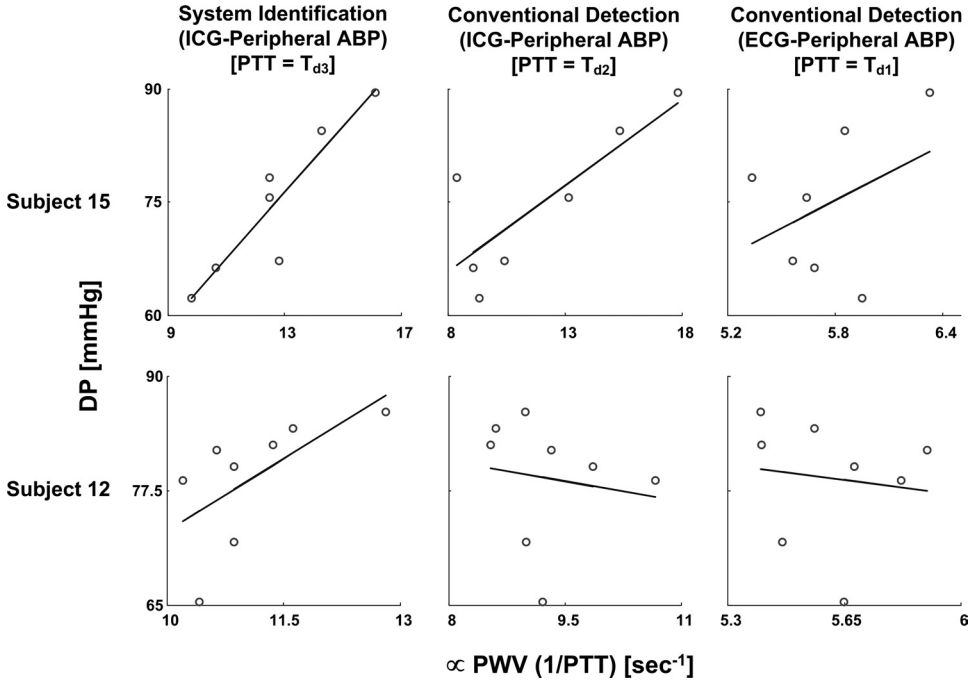

Fig. 4. Plots of measured DP vs. the proportional PWV estimated by each technique from *subjects 15* and *12*.

form artifact. The system identification approach for estimating PTT potentially provides a means to overcome both of these limitations while being applicable to arbitrary types of arterial waveforms. We applied a parametric system identification technique to noninvasive ICG and peripheral (finger) ABP waveforms measured from healthy humans during progressive LBNP. The resulting PTT estimates correlated with ABP much better than those of optimized conventional techniques. To our knowledge, these results are the first to demonstrate that the system identification approach can indeed improve PTT estimation.

System identification approach for PTT estimation. The system identification approach for PTT estimation is employed as follows. First, proximal and distal arterial waveforms are measured and respectively regarded as the input and output of a system. Next, the system impulse response is identified from the measured input and output. Finally, the time delay of the impulse response is detected as an estimate of PTT. This approach is similar in concept to previous techniques for estimating PTT that have experimentally eliminated the reflected wave by applying a transient perturbation to a proximal arterial site and then measuring the time delay for the response to occur at a distal arterial site (1, 10). However, the obvious advantage of the system identification approach is that no experimental perturbation is needed.

The system identification approach should also afford significant advantages over conventional foot-to-foot detection techniques and other previous techniques for estimating PTT without a perturbation. First, this approach effectively determines PTT from all pairs of samples of the waveforms, rather than just one pair or a few pairs, by mathematically eliminating the reflected wave or, more generally, equalizing the waveform shapes. In this way, the approach should be robust to waveform artifact while revealing the true PTT in the absence of wave

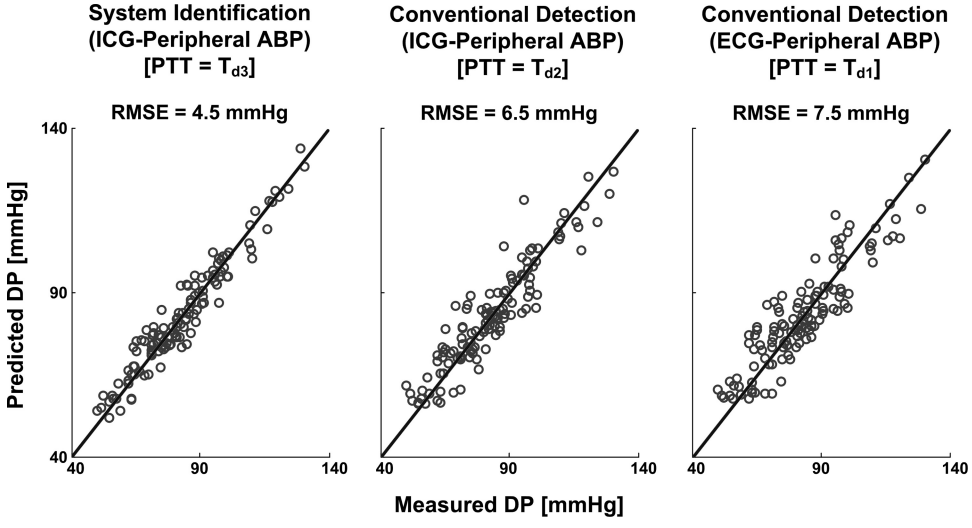

Fig. 5. Plots of the DP predicted from the proportional PWV estimates of each technique vs. measured DP from all 15 subjects. The RMSE values represent the root mean square of the errors pooled together from all of the subjects instead of the average of the RMSE values over the subjects (as shown in Table 1).

Table 1. *Results of each pulse transit time estimation technique per subject*

		System Identification (ICG-Peripheral ABP) (PTT = T_{d3})		Conventional Detection (ICG-Peripheral ABP) (PTT = T_{d2})		Conventional Detection (ECG-Peripheral ABP) (PTT = T_{d1})	
Subject No.	DP Range, mmHg	*r*	RMSE, mmHg	*r*	RMSE, mmHg	*r*	RMSE, mmHg
1	75–101	0.55	6.8	0.39	7.5	0.33	7.7
2	97–121	0.96	2.7	0.91	3.8	0.53	7.8
3	71–99	0.85	4.2	0.86	4.2	0.63	6.3
4	95–116	0.85	4.0	0.88	3.6	0.46	6.8
5	88–130	0.95	4.8	0.66	11.8	0.76	10.1
6	64–86	0.92	2.4	0.86	3.1	0.47	5.3
7	69–100	0.84	5.9	0.18	10.8	0.20	10.7
8	54–75	0.83	3.6	0.81	3.8	0.36	6.1
9	64–85	0.38	6.5	0.61	5.6	−0.89	3.2
10	65–91	0.85	4.5	0.85	4.5	0.29	8.2
11	72–95	0.91	3.3	0.71	5.4	0.35	7.2
12	65–86	0.63	5.0	−0.15	6.4	−0.13	6.4
13	50–71	0.82	3.9	−0.23	6.6	−0.12	6.8
14	62–83	0.91	3.4	0.69	5.9	0.49	7.1
15	62–89	0.92	3.7	0.81	5.5	0.39	8.6
Average	70–95	0.81 ± 0.16	4.3 ± 1.3	0.59 ± 0.37‡	5.9 ± 2.5†	0.28 ± 0.40*	7.2 ± 1.8*

Average quantities are presented as means ± SD. DP, diastolic pressure; ICG, impedance cardiography; ABP, arterial blood pressure; *r*, correlation coefficient between 1/PTT estimates and DP; RMSE, root mean squared error between DP predicted from 1/PTT estimates and measured DP. Level of statistical significance vs. system identification: *$P < 0.001$, †$P < 0.01$, and ‡$P < 0.05$. See the legend for Fig. 1 for remaining abbreviations.

reflection. The approach is therefore intended to improve the accuracy of PTT estimation rather than to make the PTT measurement process more convenient as others have proposed via an ECG or otherwise (19). Second, the system identification approach is applicable to arbitrary types of arterial waveforms, including those indicative of ABP, flow, and volume, instead of being restricted to certain types of waveforms (18). For example, the waveforms could be acquired with tonometry, ultrasound, ballistocardiography (proximal only), electrical impedance, pulse oximetry, and even noncontact laser Doppler vibrometry (8). The disadvantage of the approach is that it may not be able to estimate PTT on a beat-to-beat basis, since longer waveform segments are typically needed to reliably identify the impulse response.

Evaluation approach and limitations. Ideally, we would have evaluated the parametric system identification technique against reference measurements of PTT. However, these measurements are not simple to make. We therefore evaluated the technique in terms of the ability of its proportional PWV estimates to track changes in ABP induced by progressive LBNP. Note that the approach of evaluating PWV estimates in terms of their ability to track ABP changes is not new and originates from many studies that have shown a tight, acute relationship between PWV and ABP (9, 18).

However, we acknowledge that ABP was likely not the only significant determinant of the true PWV in this study. Indeed, vasomotor tone changes (e.g., vasoconstriction occurred during LBNP as a compensatory response), which may have altered PWV without appreciably influencing ABP, constitute the major study limitation. If PWV were estimated through the aorta, which is relatively sparse in smooth muscle (15), rather than to a finger, such changes may have been less of a factor. On the other hand, HR and cardiac output were probably not significant determinants of PWV in this study for the following reasons. First, PWV in large arteries is essentially constant across frequencies because of negligible viscous effects (16). Thus, since we investigated PWV through largely nonviscous arteries, PWV here should have been mostly independent of HR. Second, PWV characterizes the properties of the arteries only. Therefore, cardiac output could have only impacted PWV via alterations in ABP.

Although the relationship between ABP and PWV generally follows an exponential (18), it could be well approximated here as linear because of the relatively narrow ABP range elicited by the LBNP. Thus, we quantitatively evaluated the ability of the technique to track ABP changes in terms of the linear correlation between its PWV estimates and ABP.

Tracking DP. In 15 subjects, DP was perturbed appreciably (>20 mmHg) by the LBNP. In these subjects, the parametric system identification technique achieved an average *r* value between its proportional PWV estimates and measured DP of 0.81 ± 0.16 and an average RMSE value between the DP predicted from these estimates and measured DP of 4.3 ± 1.3 mmHg. These averages were ~30% better than those of an optimized version of the conventional foot-to-foot detection technique applied to the same waveforms. Furthermore, in two subjects, the system identification technique was able to profoundly "correct" the PWV estimates of the conventional technique to show appropriate positive, rather than negative, correlation with DP.

We also assessed the conventional foot-to-foot detection technique with the ECG waveform substituted for the ICG waveform. This commonly proposed technique actually estimates the sum of PTT and the preejection period (PEP). Because PEP generally changed in the opposite direction of PTT with progressive LBNP (results not shown), the technique performed poorly in tracking DP. Note that the RMSE values of this technique should be interpreted with caution. For example, in *subject 9*, the technique showed a strong, nonphysiological negative correlation between its PWV estimates and DP and consequently a small RMSE value.

Tracking other ABP parameters. The proportional PWV estimates of the parametric system identification technique may correlate best with mean ABP, as they arise from all waveform samples. However, because LBNP perturbed DP much more than mean ABP, we focused on DP tracking.

Note that the PWV estimates of the conventional techniques are designed to track DP by virtue of being derived from the waveform feet. Nevertheless, the PWV estimates of the system identification technique were able to follow DP better than those of the conventional techniques. The likely reason is that DP correlated well with mean ABP here, which is generally the case. On the other hand, SP can show less correlation to DP and mean ABP. Indeed, for those subjects whose SP changed by >20 mmHg ($n = 12$), none of techniques yielded proportional PWV estimates that were able to track SP (average r and RMSE values ranged from 0.11 ± 0.50 to 0.29 ± 0.45 and from 8.6 ± 3.6 to 9.0 ± 4.3 mmHg; P = not significant). These results are not an indictment against the system identification technique or the conventional technique applied to the same waveforms, since their PWV estimates correlated significantly better with DP. However, because the PWV estimates of the conventional technique applied to the ECG waveforms showed poor tracking of all ABP parameters, we conclude that it is not suitable during progressive central hypovolemia.

Reproducibility. In addition to accuracy, reproducibility across time in the same subjects would be another necessary attribute for the parametric system identification technique. In *subjects 1* and *4*, repeated measurements were available on a second day. We therefore conducted preliminary reproducibility testing of the technique. The overall RMSE of the PTT estimates on the second day relative to the first day was just 4.9%. Thus, the technique was highly reproducible. Furthermore, the first and second day r values between the proportional PWV estimates and measured DP were 0.55 and 0.51 in one of the subjects and 0.85 and 0.80 in the other subject. Thus, the evaluation results of the technique were also reproducible. For the conventional techniques, the corresponding reproducibility results were generally not as strong. For example, the overall RMSE values of their PTT estimates between the two days were ~13% each.

Future directions and potential clinical applications. Further investigation of the system identification approach for PTT estimation is warranted. First and foremost, testing of the approach in patients recommended for PWV monitoring (e.g., elderly, hypertensives) is a must. Thorough reproducibility testing also remains to be performed. In addition, refinements to the specific technique described herein via other system identification and time-delay estimation techniques (3) are also needed to reduce or even eliminate instances of poor performance (i.e., *subject 9*).

With successful future efforts, the system identification approach for PTT estimation may be employed for improved arterial stiffness monitoring in hypertension patients. For example, consistent with common practice (14), this approach could be applied to noninvasive carotid and femoral ABP waveforms obtained with tonometry in these patients for more accurate PWV estimation and thus potentially superior prognostic information (although nontrivial PWV error may still be present because of transit distance measurement inaccuracy). The approach could also be applied to arterial waveforms acquired with simple sensors (e.g., carotid artery and toe pulse oximeters) for potentially accurate, continuous, noninvasive, and cuffless ABP monitoring. However, other problems, including convenient construction of patient-specific calibration curves relating DP and mean ABP to PWV as well as SP estimation, must be solved before it could be used for such convenient ABP monitoring.

GRANTS

This work was supported by National Science Foundation CAREER Grant 0643477 and by the Telemedicine and Advanced Technology Research Center at the U.S. Army Medical Research and Materiel Command through Award W81XWH-10-2-0124.

DISCLOSURES

None.

REFERENCES

1. **Anliker M, Histand MB, Ogden E.** Dispersion and attenuation of small artificial pressure waves in the canine aorta. *Circ Res* 23: 539–551, 1968.
2. **Asmar R.** *Arterial Stiffness and Pulse Wave Velocity. Clinical Applications*. St. Louis, MO: Elsevier, 1999.
3. **Bjorklund S.** *A survey and comparison of time-delay estimation methods in linear systems* (online). http://www.control.isy.liu.se/publications/doc?id=1599 [12 March, 2011].
4. **Blacher J, Asmar R, Djane S, London GM, Safar ME.** Aortic pulse wave velocity as a marker of cardiovascular risk in hypertensive patients. *Hypertension* 33: 1111–1117, 1999.
5. **Boutouyrie P, Briet M, Collin C, Vermeersch S, Pannier B.** Assessment of pulse wave velocity. *Artery Res* 3: 3–8, 2009.
6. **Chiu YC, Arand PW, Shroff SG, Feldman T, Carroll JD.** Determination of pulse wave velocities with computerized algorithms. *Am Heart J* 121: 1460–1470, 1991.
7. **Convertino VA, Ryan KL, Rickards CA, Salinas J, McManus JG, Cooke WH, Holcomb JB.** Physiological and medical monitoring for en route care of combat casualties. *J Trauma* 64: S342–S353, 2008.
8. **De Melis M, Morbiducci U, Scalise L, Tomasini EP, Delbeke D, Baets R, Van Bortel LM, Segers P.** A noncontact approach for the evaluation of large artery stiffness: a preliminary study. *Am J Hypertens* 21: 1280–1283, 2008.
9. **Geddes LA, Voelz MH, Babbs CF, Bourland JD, Tacker WA.** Pulse transit time as an indicator of arterial blood pressure. *Psychophysiology* 18: 71–74, 1981.
10. **Landowne M.** A method using induced waves to study pressure propagation in human arteries. *Circ Res* 5: 594–601, 1957.
11. **Latson TW, Hunter WC, Katoh N, Sagawa K.** Effect of nitroglycerin on aortic impedance, diameter, and pulse-wave velocity. *Circ Res* 62: 884–890, 1988.
12. **Laurent S, Boutouyrie P, Asmar R, Gautier I, Laloux B, Guize L, Ducimetiere P, Benetos A.** Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. *Hypertension* 37: 1236–1241, 2001.
13. **Ljung L.** *System Identification: Theory for the User*. Englewood Cliffs, NJ: Prentice Hall, 1987.
14. **Mancia G, De Backer G, Dominiczak A, Cifkova R, Fagard R, Germano G, Grassi G, Heagerty AM, Kjeldsen SE, Laurent S, Narkiewicz K, Ruilope L, Rynkiewicz A, Schmieder RE, Boudier HA, Zanchetti A.** Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens* 25: 1105–1187, 2007.
15. **McDonald DA.** Regional pulse-wave velocity in the arterial tree. *J Appl Physiol* 24: 73–78, 1968.
16. **Milnor WR.** *Hemodynamics*. Baltimore, MD: Williams & Wilkins, 1989.
17. **Mitchell GF, Pfeffer MA, Finn PV, Pfeffer JM.** Comparison of techniques for measuring pulse-wave velocity in the rat. *J Appl Physiol* 82: 203–210, 1997.
18. **Pruett JD, Bourland JD, Geddes LA.** Measurement of pulse-wave velocity using a beat-sampling technique. *Ann Biomed Eng* 16: 341–347, 1988.
19. **Qasem A, Avolio A.** Determination of aortic pulse wave velocity from waveform decomposition of the central aortic pressure pulse. *Hypertension* 51: 188–195, 2008.

20. **Reisner AT, Xu D, Ryan KL, Convertino VA, Rickards CA, Mukkamala R.** Monitoring non-invasive cardiac output and stroke volume during experimental human hypovolaemia and resuscitation. *Br J Anaesth* 106: 23–30, 2011.
21. **Sola J, Vetter R, Renevey P, Chetelat O, Sartori C, Rimoldi SF.** Parametric estimation of pulse arrival time: a robust approach to pulse wave velocity. *Physiol Meas* 30: 603–615, 2009.
22. **Woltjer HH, Bogaard HJ, de Vries PMJM.** The technique of impedance cardiography. *Eur Heart J* 18: 1396–1403, 1997.
23. **Xu D, Ryan KL, Rickards CA, Zhang G, Convertino VA, Mukkamala R.** Robust pulse wave velocity estimation by application of system identification to proximal and distal arterial waveforms. In: *Proc 32nd Annu Int Conf IEEE EMBS* 1: 3559–3562, 2010.